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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 024754-0114

In re patent application of

Ke-Wen DONG, et al

Serial No. 09/252,828 Group Art Unit: 1641

Filed: February 19, 1999 Examiner: Lisa Cook

For: RECOMBINANT BIOLOGICALLY ACTIVE HUMAN ZONE PELLUCIDA PROTEINS 3 (HZP3) TO TEST MAIL FERTILITY

PRELIMINARY REMARKS

Commissioner for Patents
Washington, D.C. 20231

Sir:

Rejections for Indefiniteness

The Examiner has found the use of the term "acrosome reaction" to be indefinite. Applicants define an acrosome reaction as the release of an egg-penetrating enzyme by a spematozoa and submit that this definition would be understood by one of skill in the art.

Rejections for Anticipation

Applicants contend the outstanding rejections for anticipation are erroneous and should be withdrawn. In order for a claim to be anticipated by a reference, the reference must teach all of the elements of a claim; however, none of the references cited by the Examiner teach all of the claim elements.

Description of the Dean Patents, the References Used for Rejections for Anticipation

The Examiner has rejected all claims for lack of novelty in light of U.S. Patent Nos. 5,641,487 and 5,672,488 to Dean *et al.*, both of which have identical disclosures. The Dean patents disclose the amino acid sequence of the human zona pelucida protein 3 ("ZP3"). Dean was primarily interested in using ZP3 as an epitope that, in immunological terms, invoked production of a contraceptive antibody. Accordingly, Dean constructed a λgt11-expression-vector epitope library of random ZP3 fragments and screened the library with an

anti-ZP3 antibody. The screening revealed a 16 amino acid sequence epitope of residues 327 – 342 (SEQ ID 11). A contraceptive vaccine then was made, using a solid-phase synthesizer to create a synthetic polypeptide of these residues, which was not glycosylated subsequently. See column 27, line 32, to column 29, line 24. When the synthetic polypeptide was injected into a female mouse, anti-ZP3 antibodies were raised, thus allowing for a temporary contraceptive effect.

The Dean patents do not provide an extensive listing of other useful amino acid fragments of the ZP3 protein. Besides the epitope represented by residues 327 - 342, the specification identifies a seven-residue fragment (335 - 341) as an example of an area that could be a useful epitope. See column 21, lines 20 – 43. Thus, the Dean patent discloses a total of four sequences related to human ZP3 protein: (1) the ZP3 cDNA sequence, (2) the ZP3 amino acid sequence (3) an epitope of residues 327 - 342, and (4) residues 335 – 341, which are identified as being useful as a potential epitope.

Arguments Regarding Rejections for Anticipation

Applicants urge that the Dean patents do not anticipate the present claims for several reasons. First, all of the present claims are directed to "a glycoproteins," while the fragments of Dean are synthetic peptides or peptides expressed by phages, neither of which would not be glycosylated. Accordingly, the epitope cannot be a "glycoprotein" and anticipate any of the claims. Second, the amino acid sequences of the Dean epitope and those of SEQ ID NO: 2 are significantly different due to their respective lengths. The Dean epitope residues 327 - 342 is 16 residues while SEQ ID NO: 2 is 41 residues. The homology between these two sequences is 39%, which is too low of a similarity for the sequences to be the same.[1] In fact, pending independent claims 50, 57, and 65 recite sequences that are "more than 54% homologous" to SEQ ID NO: 2, thereby further distinguishing these claims from the epitope of Dean. Third, the pending claims contain other recitations, such as to "40% to 60% carbohydrate by weight" or "expressed by a human ovarian cell line," which are not present in the Dean patents. Accordingly, as these recitations are not disclosed in the Dean patents, the rejections for lack of novelty are improper and should be withdrawn.

[1] Homology is the extent to which sequences are identical. In this case out of 41 residues of SEQ ID NO: 2, only 16 are identical with the epitope. 16/41 = 39% homology.

Arguments Regarding Functional Recitations

Finally, the Examiner has argued that the recitation of "can bind to human spermatozoa at least 10 times as strong as an equivalent molar amount of mouse ZP3," was not given any consideration because of the use of the term "can." In response, applicants have rephrased this recitation to read "that binds to human spermatozoa at least 10 times as strong as an equivalent molar amount of mouse ZP3."

Applicants urge that functional recitations can be used in claims. In support of this proposition, applicants reproduced Section 2173.05(g) of the MPEP (ed. 8), which addresses the use of functional language.

> **2173.05(g) Functional Limitations**
>
> A functional limitation is an attempt to define something by what it does, rather than by what it is (e.g., as evidenced by its specific structure or specific ingredients). There is nothing inherently wrong with defining some part of an invention in functional terms. Functional language does not, in and of itself, render a claim improper. *In re Swinehart*, 439 F.2d 210, 169 USPQ 226 (CCPA 1971).
>
> A functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. A functional limitation is often used in association with an element, ingredient, or step of a process to define a particular capability or purpose that is served by the recited element, ingredient or step. Whether or not the functional limitation complies with 35 U.S.C. 112, second paragraph is a different issue from whether the limitation is properly supported under 35 U.S.C. 112, first paragraph or is distinguished over the prior art. A few examples are set forth below to illustrate situations where the issue of whether a functional limitation complies with 35 U.S.C. 112, second paragraph was considered.
>
> It was held that the limitation used to define a radical on a chemical compound as "incapable of forming a dye with said oxidizing developing agent" although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought. *In re Barr*, 444 F.2d 588, 170 USPQ 33 (CCPA 1971).
>
> In a claim that was directed to a kit of component parts capable of being assembled, the Court held that limitations such as "members adapted to be positioned" and "portions . . . being resiliently dilatable whereby said housing may be slidably positioned" serve to precisely define present structural attributes of interrelated component parts of the claimed assembly. *In re Venezia*, 530 F.2d 956, 189 USPQ 149 (CCPA 1976).

Rejections for Obviousness

We also believe that the Examiner's rejections for obviousness are erroneous. To demonstrate obviousness, the Examiner must establish (1) motivation to combine or modify references, (2) a reasonable expectation of success and (3) a teaching or suggestion of all the elements of the claims. The Examiner's rejections fail to establish any of these elements.

Description of References Used for Rejections for Obviousness

The Examiner rejected the product by process claims, now pending as claims 57-59, as obvious over the Dean patents in view of Chamberlain *et al.*, *Proc. Nat'l Acad. Sci. USA*, Vol. 87, pp. 6014-6108, 1990) and U.S. Patent No. 5,869,053. The disclosure the Dean patents is described above. The Chamberlain reference reports the full length cDNA of human ZP3. The '053 patent mentions the PA-1 cell line in the context of testing these cells, along with many other cell types, for reactivity with an antibody to the 5T4 glycoprotein.

Arguments Regarding Rejections

As discussed above, the Dean patents fail to teach all elements of the claims, and neither Chamberlain nor the '053 patent remedies these deficiencies. Chamberlain merely teaches the cDNA sequence of human ZP3, which Dean also discloses. The '053 patent is cited by the Examiner to show that the PA-1 cell line was known in the art; however, there is no suggestion of using human ovarian cell lines to express glycoproteins. Therefore, the combination of these references fails to teach or suggest all the elements of claims 57-59.

Moreover, as none of these references discuss the expression of "a sequence that is more than 54% homologous with SEQ ID NO: 2" or transducing such a sequence from "a human ovarian cell line," one of ordinary skill in the art would not have motivation to combine or modify references or have a reasonable expectation of success.

Applicants await an Office Action on the merits.

Respectfully submitted,

August 14, 2002
Date

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